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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,695	01/28/2002	Samuel J. Danishefsky	2003080-0089	5540

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EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 10/22/2002 9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/058,695	Applicant(s) DANISHEFSKY ET AL.	
	Examiner Taofiq A. Solola	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *59,61-64,66-80,82-87 and 89-122* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *59,64,66-80,82-87 and 89-122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 59, 61-64, 66-80, 82-87, 89-122, are pending in this application.

Claims 1-58, 60, 65, 81, 88, are canceled.

Claim Rejections - 35 USC § 112

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 75-79, 85-87, 89-95, 115-116, 121-122, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing apoptosis (cell death) of cancer or tumor cells, does not reasonably provide enablement for their "inhibition". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The asserted utility is not believable on it's face. There is no known epothilone for the inhibition of cancer or tumor cells, and the specification does not provide sufficient enabling disclosure for the claimed utility.

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988):

1) Breadth of claims.

2) Nature of invention.

3) State of prior art.

4) Level of ordinary skill in the art.

5) Level predictability in the art.

6) Amount of direction and guidance provided by the inventor.

7) Existence of working examples.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breath of the claimed invention involves the use of epothilones. The nature of the invention is in the field of medicinal chemistry wherein, applicant is claiming the methods of use of epothilones for the "inhibition" of cancer or tumor cells.

The state of the prior art is what prior art knows about the nature of the invention. There is no known prior art claiming the inhibition of cancer or tumor cells by epothilones. The level of ordinary skill in the art is high but, only in the art of inducing apoptosis of cancer or tumor cells. The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. The lower the predictability, the higher the direction and guidance that must be provided by applicant. In the instant invention the predictability is very low and consequently, the need for higher levels of direction and guidance by applicant. However, the amount of direction and guidance provided by applicant is limited to assays involving only the induction of apoptosis in cancer or tumor cells. There is no evidence in the specification that established correlation between the experiments and inhibition of cancer or tumor cells. See Ex parte Mass, 9 USPQ2d 1746, 1987. The quantity of experimentation required to use the compounds as claimed in the instant invention, based on applicants limited disclosure would be undue burden because, one of ordinary skill in the art would have to perform significant amount of in-vivo experiments as well as additional in-vitro assays. By deleting "inhibition" from the claims, the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 75-79, 85-87, 89-95, 115-116, 121-122, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "killing," line 1, and "kill," line 3, claim 87 and line 2, claim 95, are not consistent with induction of apoptosis by epothilone. Therefore, claims 75-79, 85-87, 89-95, 115-116, 121-122, are indefinite. By replacing the terms with "apoptosis" the rejection would be overcome.

Applicant's arguments filed 7/19/02 have been fully considered but they are not persuasive. Applicant argues that the specification, pages 63-87, tables 5, 7, 11-13, support methods of killing and inhibition of tumor cells by epothilone. This is not persuasive because the results in tables 5, 7, 11-13, in fact support apoptosis, not killing or inhibition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59, 61-64, 66-80, 82-87, 89-122, are rejected under 35 U.S.C. 103(a) as being unpatentable over Bollag et al., Cancer Res., Vol. 55 (1995), pages 2325-2333.

Applicants claim composition of epothilone and methods of use for treating cancer or tumors particularly drug-resistant cells. In preferred embodiments, the epothilone composition further comprises at least one cytotoxic agent. Applicants also claim variable effective amounts of the epothilones, such as, from about 0.001 to about 40 mg/kg of body weight, and administration of the effective dose to a subject multiple times.

Determination of the scope and content of the prior art (MPEP §2141.01)

Bollag et al., teach epothilones A and B, their compositions as oily residue (column 2, page 2326) and methods of use for treating cancer or tumor and particularly multiple drug-resistant cells. See column 2, page 2331. Bollag et al., also teach the method of use of epothilones in combination with taxol (a cytotoxic agent). See column 2, page 2328 to column 1, page 2330.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant invention and that of Bollag et al., is that applicants are claiming effective amounts of epothilones from about 0.001 to about 40 mg/kg of body weight, and administration of the effective dose to a subject multiple times.

Finding of prima facie obviousness---rational and motivation (MPEP §2142.2413)

For Bollag et al., to use epothilones for the treatment of cancer or tumors, effective amount must necessarily be used. Also, claiming variable effective amounts of epothilones, and administration of the effective dose to a subject multiple times, is not in and of itself patentable over the prior art of Bollag et al. Administration of effective amount of a drug at different times, in the treatment of cancer is well known in the art of medicine.

Therefore, the instant invention is prima facie obvious from the teaching(s) of Bollag et al. One of ordinary skill in the art would have known to claim effective amounts of epothilones, and administration of the effective dose to a subject multiple times, at the time the instant invention was made. The motivation is in the expectation that epothilone compositions would be effective for the treatment of cancer given the experimentation performed by Bollag et al., and results thereof.

Applicant's arguments filed 7/19/02 have been fully considered but they are not persuasive. Applicant argues that Bollag et al., do not teach preparation of the composition comprising effective amounts for treating cancer, that there is no expectation of success from Bollag et al., teaching, and that there is no evidence that epothilone A or B would inhibit cancer in animal model. These are not persuasive for reasons set forth above.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 59, 61-64, 66-80,82-87, 89-95, are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 61, 69-70, 74, 83-94, 98, 106-112, 116, 124-129, 131-132, 134, 136-137, 139-140, 142-143, of co-pending Application No. 09/874,514. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicant's arguments filed 7/19/02 have been fully considered but they are not persuasive. Applicant argues that the instant application contains invention drawn to genus of epothilone compounds while application 09/874,514, is drawn to individual species or subgenus of epothilone compounds. The rejection is now amended to include only claims drawn to epothilones A and B, which are embraced by the invention of application 10/058,695.

Applicant also filed a terminal disclaimer. This is not persuasive because the filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Objection

Claims 59, 61-63, 96-108, are objected to under 37 CFR 1.75 as being substantial duplicates. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Reciting or changing the effective amount is not a further limitation in a composition claim. The limitation in a composition claim relates to the structure(s) of the active ingredient. Above claims comprise the same compounds having different effective amounts. By deleting all the duplicates the objection would be overcome.

IDS

The IDS filed 7/19/02 has been placed in the application but not considered because, none of the references listed therein is received.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Taofiq A. Solola whose telephone number is (703) 308-4690. The examiner is on flexible work schedule and the best days to get him are Mondays, Wednesdays and Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (703) 308-4537. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

TAOFIQ SOLOLA
PRIMARY EXAMINER
Group 1626

October 16, 2002